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Global dynamics of an SEI model with acute and chronic stages☆

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Abstract

A model with acute and chronic stages in a population with exponentially varying size is proposed. An equivalent system is obtained, which has two equilibriums: a disease-free equilibrium and an endemic equilibrium. The stability of these two equilibriums is controlled by the basic reproduction number R_0. When $R_0 < 1$, the disease-free equilibrium is globally stable. When $R_0 > 1$, the disease-free equilibrium is unstable and the unique endemic equilibrium is locally stable. When $R_0 > 1$ and $\gamma = 0$, $\alpha = 0$, the endemic equilibrium is globally stable in Γ^0.

MSC: 92D30; 34D23

Keywords: Epidemic model; Acute and chronic stages; Global stability; Basic reproduction number

1. Introduction

The impact of a chronic stage on the disease transmission and behavior in an exponentially growing or decaying population is the focus of this paper. The framework is applied to the case of hepatitis C, a disease characterized by a long chronic stage. Hepatitis C, previously referred to as 'non-A, non-B' hepatitis, is a viral infection of the liver which was first recognized as a separate disease in 1975. The majority of patients with acute hepatitis C develop a chronic infection which is characterized by detection of HCV RNA for a period of at least 6 months after a newly acquired infection. The most common symptoms of acute hepatitis C are fatigue and jaundice. However, the vast majority of cases (up to 90%), including those with chronic disease, are asymptomatic. This makes the diagnosis of hepatitis C very difficult and is the reason why the HCV epidemic is often called 'the silent epidemic' [1]. No vaccine is available for hepatitis C. The high mutability of the hepatitis C genome [4] complicates its development. There is no evidence that the successful treatment of HCV gives any kind of partial or temporary immunity. Hence, the models developed fall within the class of models that treated or recovered individuals move back to the susceptible class.

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Several studies exist treating epidemics in populations with active demographic patterns, particularly in the ODE case [3,2,10,7,12]. The epidemic contact process or the force of infection is typically assumed to be modeled by proportionate mixing. Derrick and van den Driessche [6] discuss a general SIRS disease transmission model in which the population varies and the rate at which susceptibles become infective is given by a rather general non-linear function. Another model with general contact function is treated in [17] where the effective contact rate is an arbitrary function of the total population size. The rate of transmission used here allows for the possibility of generation of secondary infections via contacts with two types of infectious individuals: those with acute and those with chronic infections.

Very little analysis of diseases with chronic stage has been performed. As we know, the only work was studied by [16]. A model structured by age-since-infection has also been discussed in relation to HIV in [18,19]. Reade et al. consider an ODE model for infections with acute and chronic phases with feline calicivirus [16]. Their work is mostly numerical and concentrates on the impact of vaccination on the acute and chronic phases. A model without exposed class is structured in [15], which obtained the proportional stability of the equilibriums. In this paper, it is assumed that, after the initial infection, a host stays in a latent period before becoming infectious. A four-dimensional model with acute and chronic stages is presented. The epidemic is transmitted through people's direct contacts. We suppose that the disease has a exposed period and then the patients enter into the acute stage and finally they undergo the chronic stage. The patients have no immunity after recovering and become susceptible again. We divide the population in researched area into four classes: S—susceptible, E—exposed, I—infected with acute hepatitis C, V—infected with chronic hepatitis C. The total number in time t is $N(t) = S(t) + E(t) + I(t) + V(t)$.

Setting $s = S/N, e = E/N, i = I/N, v = V/N$ leads to an equivalent system, which has two equilibriums: a disease-free equilibrium and an endemic equilibrium. We obtain the basic reproduction number R_0 of this model, which completely decides the dynamics of this model. If $R_0 < 1$, the disease-free equilibrium is globally stable in Γ, that is to say, the disease cannot be prevalent. If $R_0 > 1$, the disease-free equilibrium is unstable and the endemic equilibrium is locally stable. If $R_0 > 1$, $\gamma = 0$ and $\alpha = 0$, the endemic equilibrium is globally stable in Γ^0, that is to say, the disease will prevail and result in the endemic.

2. The model

The basic demographic assumption is:

(i) The birth rate of the population is b $(b > 0)$ and the death rate is d $(d > 0)$.

The epidemiological assumptions are:

(ii) The disease cannot be transmitted during the exposure period.

(iii) Only the acute and chronic stages are differentiated. Patients with either acute or chronic infections are capable of transmitting the disease. Once a person contacts with a susceptible individual he must be infected. Each acutely infective and each chronically infective makes β $(\beta > 0)$ and γ $(\gamma > 0)$ contacts per unit times, and then the numbers of contacting susceptible individuals per unit times are, respectively, $\beta S/N$ and $\gamma S/N$. Hence, the incidences of the total acutely infective and the total chronically infective are, respectively, $\beta SI/N$ and $\gamma SV/N$.

(iv) ε $(\varepsilon > 0)$ and k $(k > 0)$ are, respectively, the rate of progression to acute stage from the exposed and the rate of progression to chronic stage. α $(\alpha \geqslant 0)$ is the recovery rate for the chronic state.

(v) The acute stage of infection is short and often asymptomatic and there is no possibility for treatment during this state.

(vi) Since the disease-induced death rate is relatively low, it is ignored.

Under the assumptions (i)–(vi), we construct the following model:

$$\begin{cases} S'(t) = bN - (\beta I + \gamma V)\dfrac{S}{N} - dS + \alpha V, \\ E'(t) = (\beta I + \gamma V)\dfrac{S}{N} - dE - \varepsilon E, \\ I'(t) = \varepsilon E - (d + k)I, \\ V'(t) = kI - (d + \alpha)V. \end{cases} \tag{2.1}$$

By adding the equations of system (2.1), we obtain

$$N'(t) = (b - d)N.$$

We set $r = b - d$, then $N'(t) = rN$, hence $N = N_0 e^{rt}$, therefore r gives the growth rate of the population. If $r > 0$, that is, $b > d$, the population exponentially grows, if $r < 0$, that is, $b < d$, the population exponentially decreases. The case $r = 0$ or $b = d$ implies that the population is stationary.

Setting

$$s = \frac{S}{N}, \quad e = \frac{E}{N}, \quad i = \frac{I}{N}, \quad v = \frac{V}{N},$$

system (2.1) becomes the following equivalent system:

$$\begin{cases} s'(t) = b(1 - s) - (\beta i + \gamma v)s + \alpha v, \\ e'(t) = (\beta i + \gamma v)s - (\varepsilon + b)e, \\ i'(t) = \varepsilon e - (k + b)i, \\ v'(t) = ki - (\alpha + b)v, \\ s + e + i + v = 1. \end{cases} \tag{2.2}$$

Letting $e = 1 - s - i - v$ to substitute e in the third equation of (2.2) and removing the second equation, we obtain

$$\begin{cases} s'(t) = b(1 - s) - (\beta i + \gamma v)s + \alpha v, \\ i'(t) = \varepsilon(1 - s - i - v) - (k + b)i, \\ v'(t) = ki - (\alpha + b)v, \\ e = 1 - s - i - v, \\ s(0) = s_0, \quad i(0) = i_0, \quad v(0) = v_0, \end{cases} \tag{2.3}$$

where s_0 is a positive constant, i_0 and v_0 are non-negative constants. If only we can understand system (2.3), then using $e = 1 - s - i - v$ we can acquire the dynamics of system (2.2).

Set $\Gamma = \{(s, i, v) \in R^3 \mid s > 0, i \geqslant 0, v \geqslant 0, s + i + v \leqslant 1\}$. Obviously Γ is an invariable set of (2.3).

Theorem 2.1. (i) *For system* (2.2), *if* $e_0 > 0$, $i_0 > 0$, $v_0 > 0$, *then*, $e(t) > 0$, $i(t) > 0$, $v(t) > 0$ *for* $t > 0$.

(ii) *For system* (2.3), *the region* $\Gamma^0 = \{(s, i, v) \in R^3_+ \mid s + i + v < 1\}$ *is a positive invariant set*.

Proof. (i) Since $s(t) \equiv 1$, $e(t) \equiv i(t) \equiv v(t) \equiv 0$ is a solution of (2.2), according to the existence and uniqueness of the solution, when $e_0 > 0$, $i_0 > 0$, $v_0 > 0$, $e(t) > 0$, $i(t) > 0$, $v(t) > 0$ for all $t > 0$.

(ii) By (i), it suffices to show that $s(t) > 0$ for $s_0 > 0$ and $\forall t > 0$, and when $s_0 > 0$, $i_0 > 0$, $v_0 > 0$ and $s_0 + i_0 + v_0 < 1$, $s(t) + i(t) + v(t) < 1$ for all $t > 0$.

It is easy to prove, $s(t) > 0$ for $s_0 > 0$ and $\forall t > 0$. In fact, we suppose that there exists a time t_0 such that $s(t_0) = 0$ for the first time, that is, $s(t_0) = 0$ and $s(t) > 0$, $t \in [0, t_0)$. Therefore, $(\mathrm{d}s/\mathrm{d}t)|_{t=t_0} \leqslant 0$. On the other hand, by the first equation of (2.3), it follows that

$$\left.\frac{\mathrm{d}s}{\mathrm{d}t}\right|_{t=t_0} = b + \alpha v > 0,$$

a contradiction.

By the second equation of (2.2)

$$e(t) = e_0 e^{-(\varepsilon+b)t} + \int_0^t (\beta i + \gamma v)s e^{-(\varepsilon+b)(t-\theta)}\,\mathrm{d}\theta > 0.$$

We also note that $s(t) + e(t) + i(t) + v(t) \equiv 1$, hence $s(t) + i(t) + v(t) < 1$ for all $t > 0$. We complete the proof. □

3. The analysis of the stability

In this section, we discuss system (2.3) in the region Γ. Evidently, system (2.3) has a disease-free equilibrium $P_0 = (1, 0, 0)$. The basic reproduction number of system (2.3) R_0 (for definition of R_0 see [14], which is critical value determining whether an endemic equilibrium exists) is defined as

$$R_0 = \varepsilon \frac{\beta(\alpha + b) + k\gamma}{(\alpha + b)(k + b)(\varepsilon + b)}.$$

When $R_0 > 1$, it has yet a unique endemic equilibrium $P^* = (s^*, i^*, v^*)$, here

$$s^* = 1 - \frac{(k + b)(\varepsilon + \alpha + b) + \varepsilon\alpha}{\varepsilon(\alpha + b)}\, i^* = \frac{1}{R_0},$$

$$i^* = \left(1 - \frac{1}{R_0}\right) \frac{\varepsilon}{\varepsilon + b}\, \frac{b(\varepsilon + \alpha + b) + \varepsilon\alpha}{(k + b)(\varepsilon + \alpha + b) + \varepsilon\alpha},$$

$$v^* = \frac{k}{\alpha + b}\, i^*,$$

where R_0 can be rewritten as

$$R_0 = \frac{\varepsilon\beta}{(k + b)(\varepsilon + b)} + \frac{\varepsilon k\gamma}{(\alpha + b)(k + b)(\varepsilon + b)}.$$

The first term $\varepsilon\beta/(k + b)(\varepsilon + b)$ can be interpreted as the contribution to the reproduction number due to secondary infections generated by an infective with acute hepatitis C. Naturally, it increases as the effective contact rate β of individuals with acute hepatitis C increases. The second term $\varepsilon k\gamma/(\alpha + b)(k + b)(\varepsilon + b)$ can be interpreted as the contribution to the reproduction number due to secondary infections generated by an infective with chronic hepatitis C. It increases with the increase of effective contact rate of chronic individual, γ. The reproduction number R_0 has a more complicated response to variations of the rate of progression to chronic stage, k. Because

$$\frac{\mathrm{d}R_0}{\mathrm{d}k} = \varepsilon \frac{b(\gamma - \beta) - \beta\alpha}{(\alpha + b)(\varepsilon + b)(k + b)^2},$$

it increases when $b(\gamma - \beta) - \beta\alpha > 0$ and decreases when the opposite inequality is valid. In particular, when $b(\gamma - \beta) - \beta\alpha = 0$, R_0 cannot change as k varies. However, the probability of transmitting the disease from an individual with acute infection is larger than that from an individual with chronic infection, that is, $\beta > \gamma$. Therefore, we expect that for realistic values of the parameters, R_0 will decrease as the rate progression to chronic stage increases.

Theorem 3.1. *When $R_0 < 1$, the disease-free equilibrium P_0 is locally stable.*

Proof. The Jacobi matrix of system (2.3) at P_0 is

$$\begin{pmatrix} -b & -\beta & -\gamma + \alpha \\ -\varepsilon & -\varepsilon - k - b & -\varepsilon \\ 0 & k & -\alpha - b \end{pmatrix}.$$

Therefore, its characteristic equation at P_0 is

$$\lambda^3 + A\lambda^2 + B\lambda + C = 0, \tag{3.1}$$

where

$$A = \alpha + \varepsilon + 3b,$$

$$B = (\alpha + b)(\varepsilon + k + 2b) + (k + b)(\varepsilon + b) - \beta\varepsilon,$$

$$C = (\alpha + b)(k + b)(\varepsilon + b) - \varepsilon[\beta(\alpha + b) + k\gamma].$$

When $R_0 < 1$, $A > 0$, $C > 0$, it follows that from $C > 0$

$$(\alpha + b)(k + b)(\varepsilon + b) - \beta\varepsilon(\alpha + b) > 0,$$

that is

$$(k + b)(\varepsilon + b) - \beta\varepsilon > 0,$$

therefore

$$B > 0.$$

In the following we will calculate $AB - C$.

$$\begin{aligned} AB - C &= (\alpha + \varepsilon + k + 3b)[(\alpha + b)(\varepsilon + k + 2b) + (k + b)(\varepsilon + b) - \beta\varepsilon] - C \\ &= (\alpha + b + \varepsilon + b + k + b)[(\alpha + b)(\varepsilon + b + k + b) + (k + b)(\varepsilon + b) - \beta\varepsilon] - C \\ &= (\alpha + b + \varepsilon + b)[(\alpha + b)(\varepsilon + b + k + b) + (k + b)(\varepsilon + b) - \beta\varepsilon] \\ &\quad + (k + b)(\alpha + b)(\varepsilon + b) + (k + b)[(\alpha + b)(k + b) + (k + b)(\varepsilon + b) - \beta\varepsilon] - C \\ &= (\alpha + \varepsilon + 2b)[(\alpha + b)(\varepsilon + k + 2b) + (k + b)(\varepsilon + b) - \beta\varepsilon] \\ &\quad + (k + b)[(\alpha + b)(k + b) + (k + b)(\varepsilon + b) - \beta\varepsilon] + \varepsilon[\beta(\alpha + b) + k\gamma] \\ &> 0. \end{aligned}$$

The last inequality is due to $R_0 < 1$. By Routh–Hurwitz theorem, the roots of equation (3.1) all have negative real parts. Therefore, when $R_0 < 1$, the disease-free equilibrium P_0 is locally stable. □

Lemma 3.2 (*see Feng et al. [8]*). *Assuming* $f : [0, \infty) \longrightarrow R$ *is bounded*, $k \in L^1(0, \infty)$, *then*

$$\limsup_{t\to\infty} \left| \int_0^t k(\theta) f(t - \theta)\, \mathrm{d}\theta \right| \leqslant |f|^\infty \|k\|_{L^1(0,\infty)},$$

where $|f|^\infty = \limsup_{t\to\infty} |f(t)|$.

Theorem 3.3. *When* $R_0 < 1$, *the disease-free equilibrium* $P_0(1, 0, 0)$ *is globally stable*.

Proof. By Theorem 3.1, it suffices to prove that P_0 is attractive globally for $R_0 < 1$. We note that the global attractive of P_0 is equivalent to that of the disease-free equilibrium $(1, 0, 0, 0)$ of system (2.2).

The second equation of (2.2) yields

$$e'(t) \leqslant (\beta i + \gamma v) - (\varepsilon + b)e.$$

Firstly, we solve the comparative equation

$$x'(t) = (\beta i + \gamma v) - (\varepsilon + b)x,$$

which yields

$$x(t) = e_0 x^{-(\varepsilon+b)t} + \int_0^t (\beta i + \gamma v) x^{-(\varepsilon+b)(t-s)}\, \mathrm{d}s.$$

By the comparative principle [13], we have

$$\limsup_{t\to\infty} e(t) \leqslant \limsup_{t\to\infty} \int_0^t [\beta i(t-s) + \gamma v(t-s)]\mathrm{e}^{-(\varepsilon+b)s}\,\mathrm{d}s.$$

From Lemma 3.2, we have

$$\begin{aligned}\limsup_{t\to\infty} e(t) &\leqslant \left[\beta \limsup_{t\to\infty} i(t) + \gamma \limsup_{t\to\infty} v(t)\right] \int_0^\infty \mathrm{e}^{-(\varepsilon+b)s}\,\mathrm{d}s \\ &= \frac{\beta}{\varepsilon+b} \limsup_{t\to\infty} i(t) + \frac{\gamma}{\varepsilon+b} \limsup_{t\to\infty} v(t). \end{aligned} \tag{3.2}$$

By the last equation of (2.2), we have

$$v(t) = \mathrm{e}^{-(b+\alpha)t} v_0 + k \int_0^t \mathrm{e}^{-(b+\alpha)s} i(t-s)\,\mathrm{d}s,$$

therefore,

$$\begin{aligned}\limsup_{t\to\infty} v(t) &\leqslant k \limsup_{t\to\infty} i(t) \int_0^\infty \mathrm{e}^{-(b+\alpha)s}\,\mathrm{d}s \\ &= \frac{k}{b+\alpha} \limsup_{t\to\infty} i(t). \end{aligned} \tag{3.3}$$

Substituting $\limsup_{t\to\infty} e(t)$ of inequality (3.2) for the right side of the inequality (3.3) yields

$$\limsup_{t\to\infty} e(t) \leqslant \frac{\beta}{\varepsilon+b} \limsup_{t\to\infty} i(t) + \frac{\gamma k}{(b+\varepsilon)(b+\alpha)} \limsup_{t\to\infty} i(t). \tag{3.4}$$

By the second equation of (2.2), we obtain

$$i(t) = i_0 \mathrm{e}^{-(k+b)s} + \varepsilon \int_0^t e(s)\mathrm{e}^{-(k+b)(t-s)}\,\mathrm{d}s.$$

Therefore,

$$\limsup_{t\to\infty} i(t) \leqslant \frac{\varepsilon}{k+b} \limsup_{t\to\infty} e(t). \tag{3.5}$$

Noting inequality (3.4), we have

$$\begin{aligned}\limsup_{t\to\infty} e(t) &\leqslant \left[\frac{\beta\varepsilon}{(\varepsilon+b)(k+b)} + \frac{\varepsilon\gamma k}{(b+\varepsilon)(b+\alpha)(b+k)}\right] \limsup_{t\to\infty} e(t) \\ &= R_0 \limsup_{t\to\infty} e(t). \end{aligned} \tag{3.6}$$

By $R_0 < 1$ and (3.6), we have $\limsup_{t\to\infty} e(t) = 0$ and $\lim_{t\to\infty} e(t) = 0$. By inequality (3.5) and (3.3), we have

$$\lim_{t\to\infty} i(t) = 0, \quad \lim_{t\to\infty} v(t) = 0.$$

From $s(t)+e(t)+i(t)+v(t)=1$, it follows that $\lim_{t\to\infty} s(t)=1$. Therefore, when $R_0 < 1$, the disease-free equilibrium $P_0(1, 0, 0)$ is globally stable. □

Theorem 3.3 indicates that the epidemic cannot be prevalent only if R_0 is smaller than 1. From the above analysis, we know that R_0 will decrease when β and γ decrease or k increases. Numerical simulations confirm that the disease-free equilibrium P_0 is asymptotically stable as proved in Theorem 3.3 (see Fig. 1).

Theorem 3.4. *When $R_0 > 1$, the disease-free equilibrium P_0 is unstable, the endemic equilibrium P^* is locally stable.*

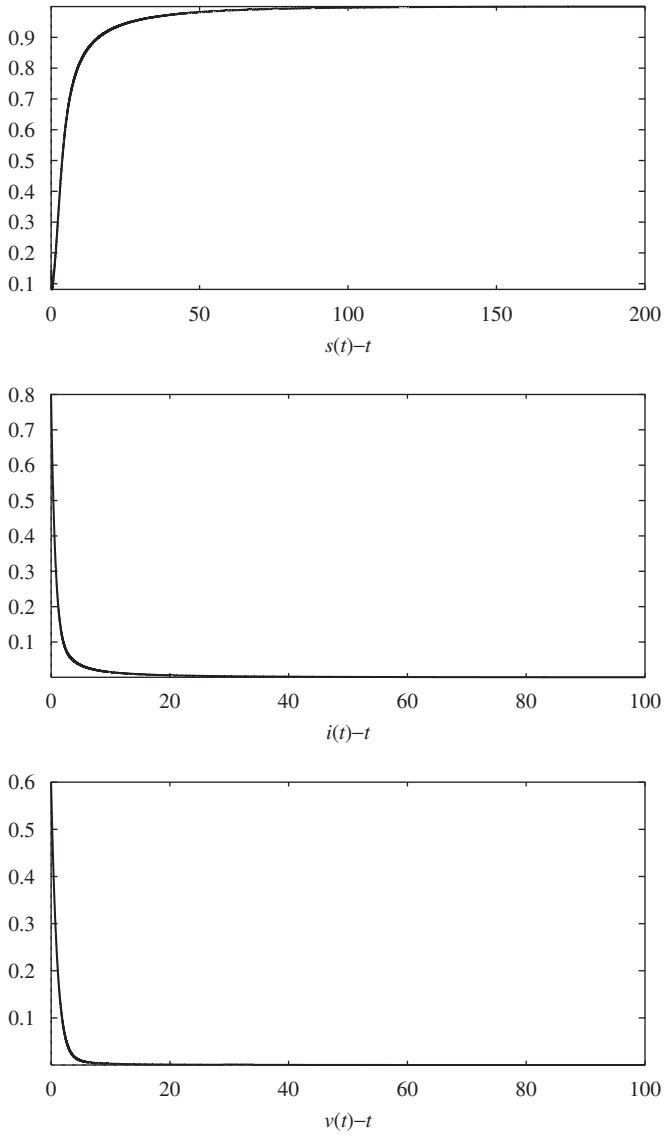

Fig. 1. When $\beta = 10$, $\gamma = 15$, $b = 1$, $\alpha = k = 0.2$, $\varepsilon = 0.1$, that is, $R_0 = \frac{15}{15.84} < 1$, disease-free equilibrium P_0 is asymptotically stable.

Proof. When $R_0 > 1$, the coefficient C of equation (3.1) is smaller than 0, by Routh–Hurwitz theorem, the disease-free equilibrium is unstable.

The Jacobi matrix of system (2.3) at P^* is

$$\begin{pmatrix} -b - (\beta i^* + \gamma v^*) & -\beta s^* & -\gamma s^* + \alpha \\ -\varepsilon & -\varepsilon - (k + b) & -\varepsilon \\ 0 & k & -(\alpha + b) \end{pmatrix},$$

therefore, its characteristic equation at P^* is

$$\lambda^3 + E\lambda^2 + F\lambda + G = 0,$$

where

$$E = \beta i^* + \gamma v^* + \varepsilon + k + \alpha + 3b,$$

$$F = (\alpha + b)(\beta i^* + \gamma v^* + \varepsilon + k + 2b) + (\beta i^* + \gamma v^* + b)(\varepsilon + k + b) - \varepsilon\beta s^* + k\varepsilon,$$

$$G = (\alpha + b)[(\beta i^* + \gamma v^* + b)(\varepsilon + k + b) - \varepsilon\beta s^*] + k[\varepsilon(\alpha + b) + \varepsilon(\beta i^* + \gamma v^*) - \varepsilon\gamma s^*].$$

Evidently $E > 0$, establishing the sign of G in the following:

$$\begin{aligned} G &= (\alpha + b)(\varepsilon + k + b)(\beta i^* + \gamma v^*) + b(\alpha + b)(\varepsilon + k + b) - \varepsilon\beta(\alpha + b)s^* \\ &\quad + k\varepsilon(\alpha + b) + k\varepsilon(\beta i^* + \gamma v^*) - k\varepsilon\gamma s^* \\ &= (\alpha + b)[b(\varepsilon + k + b) + k\varepsilon] + [(\alpha + b)(\varepsilon + k + b) + k\varepsilon](\beta i^* + \gamma v^*) \\ &\quad - \varepsilon[\beta(\alpha + b) + k\gamma]s^* \\ &= (\alpha + b)(k + b)(\varepsilon + b) + [(\alpha + b)(\varepsilon + k + b) + k\varepsilon](\beta i^* + \gamma v^*) \\ &\quad - \varepsilon[\beta(\alpha + b) + k\gamma]s^* \\ &= [(\alpha + b)(\varepsilon + k + b) + k\varepsilon](\beta i^* + \gamma v^*) \\ &> 0. \end{aligned}$$

The last equality is due to $s^* = 1/R_0$.

In the following, we calculate the sign of $EF - G$, to do this, we calculate $\beta i^* + \gamma v^*$ firstly:

$$\begin{aligned} \beta i^* + \gamma v^* &= \beta i^* + \frac{\gamma k}{\alpha + b} i^* \\ &= \frac{(R_0 - 1)(k + b)(\alpha + b)(\varepsilon + b)}{(k + b)(\varepsilon + \alpha + b) + \varepsilon\alpha}. \end{aligned}$$

Noting $s^* = 1/R_0$ and F, we calculate $EF - G$ and we get the denominator of $EF - G$ as $R_0[(k+b)(\varepsilon+\alpha+b)+\varepsilon\alpha]^2$, which is larger than 0. Consequently, the sign of $EF - G$ is the same as its numerator, which is denoted by a, then

$$\begin{aligned} a &= R_0(\varepsilon + k + \alpha + 2b)(R_0 - 1)^2(k + b)^2(\alpha + b)^2(\varepsilon + b)^2 \\ &\quad + R_0(R_0 - 1)(b + k)(\alpha + b)(\varepsilon + b)[(k + b)(\varepsilon + k + b) + k\varepsilon] \\ &\quad \times [(\varepsilon + k + \alpha + 2b)(\varepsilon + k + \alpha + 3b) - (\alpha + b)(\varepsilon + k + b) - k\varepsilon] \\ &\quad + (R_0 - 1)(b + k)(\alpha + b)(\varepsilon + b)[(k + b)(\varepsilon + \alpha + b) + \varepsilon\alpha] \\ &\quad \times [R_0(\alpha + b)(\varepsilon + k + 2b) + R_0(\varepsilon + b)(k + b) - \beta\varepsilon] \\ &\quad + (\varepsilon + k + \alpha + 3b)[(k + b)(\varepsilon + \alpha + b) + \varepsilon\alpha]^2 \\ &\quad \times [R_0(\alpha + b)(\varepsilon + k + 2b) + R_0(\varepsilon + b)(k + b) - \beta\varepsilon]. \end{aligned}$$

Obviously, $(\varepsilon + k + \alpha + 2b)(\varepsilon + k + \alpha + 3b) - (\alpha + b)(\varepsilon + k + b) - k\varepsilon > 0$.

Since $R_0 > \beta\varepsilon/(\varepsilon + b)(k + b)$ and $R_0 > 1$, the third and the fourth terms of a are both positive, then it follows that $EF - G > 0$. By Routh–Hurwitz theorem, it follows from $R_0 > 1$ that P^* is locally stable. □

Letting $v = 1 - s - e - i$ to substitute the v of the first and the second equations in (2.2), system (2.2) becomes

$$\begin{cases} s'(t) = b(1-s) - \beta i s - \gamma s(1-s-e-i) + \alpha(1-s-e-i), \\ e'(t) = \beta i s + \gamma s(1-s-e-i) - (\varepsilon + b)e, \\ i'(t) = \varepsilon e - (k+b)i, \\ v = 1 - s - e - i. \end{cases} \tag{3.7}$$

Set

$$\Omega = \{(s, e, i) \in R_+^3 | s + e + i < 1\}.$$

Let $x \to f(x) \in \mathbf{R}^n$ be a C^1 function for x in an open set $D \subset \mathbf{R}^n$. Consider the differential equation

$$x' = f(x). \tag{3.8}$$

Denote by $x(t, x_0)$ the solution to (3.8) such that $x(0, x_0) = x_0$. We make the following two assumptions:

(H_1) Eq. (3.8) has a unique equilibrium $\bar{x}$ in D.
(H_2) There exists a compact absorbing set $K \subset D$.

Lemma 3.5 (*see Li and Muldowney [11]*). *Under the assumptions* (H_1) *and* (H_2), *find conditions on* (3.8) *such that the local stability of* $\bar{x}$ *implies its global stability in D.*

Theorem 3.6. *When* $R_0 > 1$, *if* $\gamma = 0$, $\alpha = 0$, *then the endemic equilibrium* P^* *of system* (2.3) *is globally stable in* Γ^0.

Proof. The global stability of the endemic equilibrium P^* of system (2.3) in Γ^0 is equivalent to that of the endemic equilibrium $\bar{P}(\bar{s}, \bar{e}, \bar{i})$ of system (3.7) in Ω.

We use Lemma 3.5 to prove that the endemic equilibrium $\bar{P}$ of system (3.7) is globally stable in Ω.

Evidently, system (3.7) has unique endemic equilibrium $\bar{P}$ in Ω, hence it satisfies the assumption (H_1). Because $R_0 > 1$, the instability of P_0 and the boundedness of the solutions of system (3.7) ensure system (3.7) has a compact set in Ω, so it also satisfies the assumption (H_2).

When $\gamma = 0$, $\alpha = 0$, the Jacobian matrix of system (3.7) is

$$J = \begin{pmatrix} -b - \beta i & 0 & -\beta s \\ \beta i & -\varepsilon - b & \beta s \\ 0 & \varepsilon & -k - b \end{pmatrix},$$

and its second additive compound matrix is

$$J^{[2]} = \begin{pmatrix} -2b - \varepsilon - \beta i & \beta s & \beta s \\ \varepsilon & -2b - k - \beta i & 0 \\ 0 & \beta i & -2b - \varepsilon - k \end{pmatrix}.$$

Set the function

$$P(X) = P(s, e, i) = \operatorname{diag}\left\{1, \frac{e}{i}, \frac{e}{i}\right\},$$

then

$$P_f P^{-1} = \operatorname{diag}\left\{0, \frac{e'}{e} - \frac{i'}{i}, \frac{e'}{e} - \frac{i'}{i}\right\},$$

and the matrix $B = P_f P^{-1} + P J^{[2]} P^{-1}$ can be written in block form as

$$B = \begin{pmatrix} B_{11} & B_{12} \\ B_{21} & B_{22} \end{pmatrix},$$

where

$$B_{11} = -2b - \varepsilon - \beta i,$$

$$B_{12} = \left(\beta s \frac{i}{e}, \beta s \frac{i}{e} \right),$$

$$B_{21} = \begin{pmatrix} \varepsilon \frac{e}{i} \\ 0 \end{pmatrix},$$

$$B_{22} = \begin{pmatrix} \frac{e'}{e} - \frac{i'}{i} - 2b - k - \beta i & 0 \\ \beta i & \frac{e'}{e} - \frac{i'}{i} - 2b - \varepsilon - k \end{pmatrix}.$$

Let (u, v, w) denote the vectors in $R^3 \cong R^{\binom{3}{2}}$. We select a norm in R^3 as

$$|(u, v, w)| = \max\{|u|, |v + w|\}$$

and let μ denote the Lozinskii measure with respect to this norm. Using the method of estimating μ in [9], we have

$$\mu(B) \leqslant \sup\{g_1, g_2\}, \tag{3.9}$$

where

$$g_1 = \mu_1(B_{11}) + |B_{12}|,$$

$$g_2 = |B_{21}| + \mu_1(B_{22}).$$

Here $|B_{12}|$, $|B_{21}|$ are matrix norms with respect to the l_1 vector norm, and μ_1 denotes the Lozinskii measure with respect to the l_1 norm. More specifically,

$$\mu_1(B_{11}) = -2b - \varepsilon - \beta i,$$

$$|B_{12}| = \beta s \frac{i}{e},$$

$$|B_{21}| = \varepsilon \frac{e}{i}.$$

To calculate $\mu_1(B_{22})$, we add the absolute value of the off-diagonal elements to the diagonal one in each column of B_{22}, and then take the maximum of two sums [5]. This leads to

$$\mu_1(B_{22}) = \frac{e'}{e} - \frac{i'}{i} - 2b - k.$$

Therefore,

$$g_1 = \beta s \frac{i}{e} - 2b - \varepsilon - \beta i,$$

$$g_2 = \frac{e'}{e} - \frac{i'}{i} - 2b - k + \varepsilon \frac{e}{i}.$$

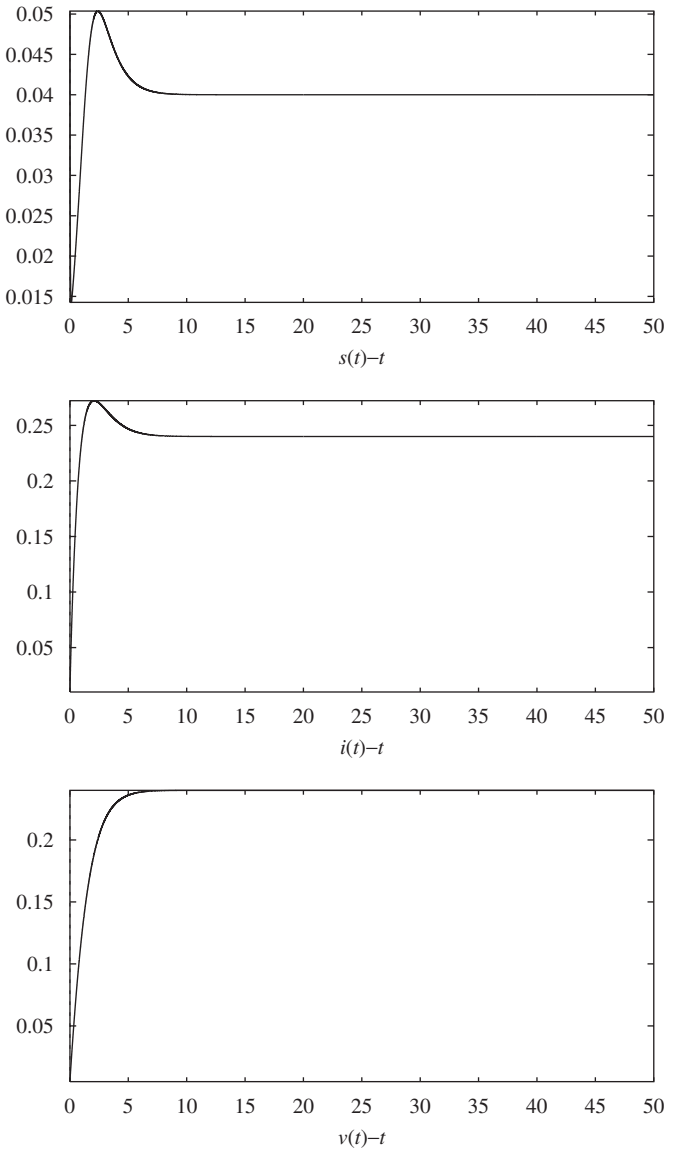

Fig. 2. When $\beta = 50$, $k = b = \varepsilon = 0.5$, that is, $R_0 = 25 > 1$, endemic equilibrium $\bar{P}$ is globally stable.

According to the second and the third equations in system (3.7), we can obtain

$$\frac{e'}{e} \geqslant \beta s \frac{i}{e} - \varepsilon - b,$$

$$\frac{i'}{i} = \varepsilon \frac{e}{i} - k - b.$$

Hence,

$$g_1 \leqslant \frac{e'}{e} - b - \beta i \leqslant \frac{e'}{e} - b,$$

$$g_2 = \frac{e'}{e} - b.$$

By (3.9) we can obtain

$$\mu(B) \leqslant \frac{e'}{e} - b.$$

Along each solution $x(t, x_0)$, $(x_0 \in K)$, where K is the compact absorbing set, we thus have

$$\frac{1}{t}\int_0^t \mu(B)\,\mathrm{d}s \leqslant \frac{1}{t}\log\frac{e(t)}{e_0} - b.$$

When $t \to \infty$, $\bar{q_2} = \limsup_{t\to\infty} \sup_{x_0\in K} \frac{1}{t}\int_0^t \mu(B(x(s, x_0)))\,ds\bar{q_2} \leqslant -b/2 < 0$.

According to the theorem of Li and Muldowney, if $\gamma = 0$, $\alpha = 0$, the endemic equilibrium $\bar{P}$ of system (3.7) is globally stable in Ω. The proof is completed. □

Numerical simulations confirm that the endemic equilibrium $\bar{P}$ is globally stable as proved in Theorem 3.6 (see Fig. 2).

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